

SEARCH REQUEST FORM

Requestor's

Name:

Rebecca Look

Serial

Number:

09/445054

Date:

7/15/04

Phone:

Rem 416 70

Art Unit:

1610

Search Topic:

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevant citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevant claim(s).

Sub: Neal Rosen

Please provide structures for all compounds of claim 54 (L27)

a) paclitaxel, taxane, epothilone A, epothilone B, desorogepothilone A, desoxyepothilone B. Are all of b) microtubule stabilizing agents.

Search preyl - protein translocase inhibitor
generically + all specific compounds of claim 54
+ each compound of b to treat cancer.
for b) - only print 2 references for each -
older than 6/4/98.

What is "atlet histiocytic lymphoma lung
ad enocarcinoma" (cl 49)

Thanks
Rebecca

STAFF USE ONLY

Date completed:

Searcher:

Terminal time:

Elapsed time:

CPU time:

Total time:

Number of Searches:

Number of Databases:

Search Site

STIC

CM-1

Pre-S

Type of Search

N.A. Sequence

A.A. Sequence

Structure

Bibliographic

Vendors

IG

1720.97 STN

Dialog

APS

Geninfo

SDC

DARC/Questel

Other

Inventor Record w/structures

Cook 09/445,054

July 26, 2004

L4 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:804132 HCAPLUS

DOCUMENT NUMBER: 130:33009

ENTRY DATE: Entered STN: 23 Dec 1998

TITLE: A method of treating cancer using an antineoplastic agent-**prenyl**-protein transferase inhibitor combination, and compound preparation

INVENTOR(S): **Rosen, Neal**; Sepp-lorenzino, Laura;
Moasser, Mark M.; Oliff, Allen I.; Gibbs, Jackson B.; Kohl, Nancy; Graham, Samuel L.; Prendergast, George C.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Sloan-Kettering Institute for Cancer Research

SOURCE: PCT Int. Appl., 379 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

INT. PATENT CLASSIF.:
MAIN: A01N043-50
SECONDARY: A01N043-60; A61K031-415; A61K031-495

CLASSIFICATION: 1-6 (Pharmacology)
Section cross-reference(s): 8, 34, 63

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9854966	A1	19981210	WO 1998-US8646	19980604
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9877957	A1	19981221	AU 1998-77957	19980604
EP 986302	A1	20000322	EP 1998-926029	19980604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2002503249	T2	20020129	JP 1999-502409	19980604
PRIORITY APPLN. INFO.:				
			US 1997-48736P	P 19970605
			GB 1998-1231	A 19980121
			WO 1998-US8646	W 19980604

ABSTRACT:

Methods are provided for treating cancer using a combination of a compound which is an antineoplastic agent and a compound which is an inhibitor of **prenyl**-protein transferase. The methods comprise administering to a mammal, either sequentially in any order or simultaneously, amts. of ≥ 2 therapeutic agents selected from a compound which is an antineoplastic agent and a compound which is an inhibitor or **prenyl**-protein transferase. The invention also relates to methods of preparing such compns.

SUPPL. TERM: **prenyl** protein transferase inhibitor
antineoplastic agent combination prepn antitumor

INDEX TERM: Microtubule
(agents stabilizing or disrupting; antineoplastic agent-**prenyl**-protein transferase inhibitor combination)

premyl- protein transferase inhib. (generic) (1998)

Cook 09/445,054

Review articles July 26, 2004

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L29 1305 SEA FILE=HCAPLUS ABB=ON PLU=ON FARNESYLTRANSFERASE/CT(L) (INHIBITORS)
B? OR ANTAG? OR BLOCK?)
L30 178659 SEA FILE=HCAPLUS ABB=ON PLU=ON ANTITUMOR AGENTS+OLD/CT
L31 873 SEA FILE=HCAPLUS ABB=ON PLU=ON L29 AND L30
L32 727 SEA FILE=HCAPLUS ABB=ON PLU=ON L31 AND (BAC OR DMA OR PAC OR PKT OR THU)/RL
L34 439 SEA FILE=HCAPLUS ABB=ON PLU=ON L32 AND P/DT
L35 288 SEA FILE=HCAPLUS ABB=ON PLU=ON L32 NOT L34
L38 81 SEA FILE=HCAPLUS ABB=ON PLU=ON L35 NOT PY>1998
L39 9 SEA FILE=HCAPLUS ABB=ON PLU=ON L38 AND REVIEW/DT
L40 9 SEA FILE=HCAPLUS ABB=ON PLU=ON L29 AND L39

=> d l40 ibib abs hitind 1-9

L40 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:73866 HCAPLUS

DOCUMENT NUMBER: 130:276077

TITLE: An update on COX-2 and farnesyltransferase inhibitor development

AUTHOR(S): Rotella, David P.

CORPORATE SOURCE: Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, NJ, 08543, USA

SOURCE: Current Opinion in Drug Discovery & Development (1998), 1(2), 165-174

CODEN: CODDF; ISSN: 1367-6733

PUBLISHER: Current Drugs Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 56 refs. on medicinal chemical and anti-inflammatory and antitumor effects of COX-2 and ras-farnesyltransferase inhibitors.

CC 1-0 (Pharmacology)

Section cross-reference(s): 27, 28

IT Antitumor agents

Drug design

Farnesylation

Medicinal chemistry

(medicinal chemical and pharmacol. of COX-2 and farnesyltransferase inhibitors)

IT 39391-18-9P

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(2, inhibitors; medicinal chemical and pharmacol. of COX-2 and farnesyltransferase inhibitors)

IT 39391-18-9P

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(2, inhibitors; medicinal chemical and pharmacol. of COX-2 and farnesyltransferase inhibitors)

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:8364 HCAPLUS

DOCUMENT NUMBER: 130:60514

TITLE: Farnesyltransferase inhibitors. A new approach to the development of potential anticancer drugs

AUTHOR(S): Schlitzer, Martin

CORPORATE SOURCE: Inst. Pharmazeutische Chemie, Philipps-Univ., Marburg, D-35032, Germany

SOURCE: Pharmazie in Unserer Zeit (1998), 27(6), 278-288

CODEN: PHUZBI; ISSN: 0048-3664

PUBLISHER: Wiley-VCH Verlag GmbH

DOCUMENT TYPE: Journal; **General Review**

LANGUAGE: German

AB A review is given with 39 refs. on farnesyltransferase inhibition as a new antitumor approach including the topics Ras signal transduction pathway, posttranslational modification of Ras proteins, farnesyltransferase, development of farnesyltransferase inhibitors.

CC 1-0 (Pharmacology)

IT **Antitumor agents**

Drug screening

Signal transduction, biological

(farnesyltransferase inhibitors, development of potential anticancer drugs)

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:740006 HCAPLUS

DOCUMENT NUMBER: 129:325626

TITLE: Novel approaches in development for the treatment of pancreatic cancer

AUTHOR(S): Butera, James; Malachovsky, Martin; Rathore, Ritesh; Safran, Howard

CORPORATE SOURCE: Departments of Med., Brown Univ., Providence, RI, USA

SOURCE: Frontiers in Bioscience [Electronic Publication]

(1998), 3, E226-E229

CODEN: FRBIF6

URL: <http://www.bioscience.org/1998/v3/e/butera/e226-229.htm>

PUBLISHER: Frontiers in Bioscience

DOCUMENT TYPE: Journal; **General Review**; (online computer file)

LANGUAGE: English

AB A review with 45 refs. Pancreatic adenocarcinomas are among the neoplasms most resistant to conventional chemotherapeutic agents. This has prompted intense investigations of novel noncytotoxic agents based on new understandings of the mol. pathobiol. of human malignancies. This review focuses on the potential uses of 3 new classes of agents: farnesyl transferase (FTPase) inhibitors, matrix metalloproteinase inhibitors (MMPis) and antibodies to the HER-2/neu oncogene. When used as single agents, FTPase inhibitors and MMPis may be cytostatic, helping to delay the growth of these cancers. All 3 classes of agents may have the greatest benefit when used in conjunction with traditional anticancer modalities. The biol. mechanisms of these agents are discussed.

CC 1-0 (Pharmacology)
IT **Antitumor agents**
 Antitumor agents
 (pancreas; novel approaches to development of)
IT Antibodies
 RL: **BAC (Biological activity or effector, except adverse);** BSU
 (Biological study, unclassified); **THU (Therapeutic use);** BIOL
 (Biological study); USES (Uses)
 (pancreatic cancer treatment with antibodies to HER-2/neu oncogene)
IT **131384-38-8, Farnesyltransferase** 141907-41-7, Matrix
 metalloproteinase
 RL: **BAC (Biological activity or effector, except adverse);** BSU
 (Biological study, unclassified); **THU (Therapeutic use);** BIOL
 (Biological study); USES (Uses)
 (**inhibitors;** pancreatic cancer treatment with)

L40 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:301907 HCAPLUS
DOCUMENT NUMBER: 129:62295
TITLE: Advances in the development of farnesyltransferase
 inhibitors: substrate recognition by protein
 farnesyltransferase
AUTHOR(S): Yang, Wenli; Villar, Keith Del; Urano, Jun; Mitsuzawa,
 Hiroshi; Tamanoi, Fuyuhiko
CORPORATE SOURCE: Department of Microbiology and Molecular Genetics,
 Jonsson Comprehensive Cancer Center, University of
 California, Los Angeles, CA, USA
SOURCE: Journal of Cellular Biochemistry (1998), Volume Date
 1997, (Suppl. 27), 12-19
 CODEN: JCEBD5; ISSN: 0730-2312
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 40 refs. A variety of compds. that show promise in cancer
 chemotherapy and chemoprevention have been identified as
 farnesyltransferase inhibitors. These can be classified into mainly two
 different types of inhibitors, farnesyl diphosphate competitors and CAAX
 peptidomimetics. The former type acts by competitively inhibiting
 farnesyltransferase with respect to one of the substrates, farnesyl
 diphosphate, whereas the latter type acts by mimicking the other
 substrate, the C-terminal CAAX motif of Ras protein. One example of a
 farnesyl diphosphate competitor is manumycin, an antibiotic detected in
 the culture media of a Streptomyces strain. The CAAX peptidomimetics were
 developed based on the unique property of farnesyltransferase to recognize
 the CAAX motif at the C-terminus of the protein substrate. The authors
 recent studies have focused on understanding the structural basis of this
 CAAX recognition. By using in vitro mutagenesis, residues of yeast
 farnesyltransferase important for the recognition of the CAAX motif have
 been identified. Two of these residues are closely located at the
 C-terminal region of the β -subunit of farnesyltransferase. These and
 other results on the structural basis of the CAAX recognition may provide
 information valuable for structure-based design of farnesyltransferase
 inhibitors.

CC 1-0 (Pharmacology)
IT **Antitumor agents**
 Drug design
 Farnesylation

Peptidomimetics

(advances in the development of farnesyltransferase inhibitors)

IT 52665-74-4, Manumycin A 141400-83-1, SCH44342 156511-34-1, L 739749
157479-39-5, B 581 170006-72-1, FTI-276

RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); **THU (Therapeutic use)**; BIOL
(Biological study); USES (Uses)

(advances in the development of farnesyltransferase inhibitors)

IT 13058-04-3, Farnesyl diphosphate

RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); **THU (Therapeutic use)**; BIOL
(Biological study); USES (Uses)

(competitors; advances in the development of farnesyltransferase inhibitors)

IT 13058-04-3, Farnesyl diphosphate

RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); **THU (Therapeutic use)**; BIOL
(Biological study); USES (Uses)

(competitors; advances in the development of farnesyltransferase inhibitors)

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:403757 HCAPLUS

DOCUMENT NUMBER: 127:130255

TITLE: Inhibition of Ras prenylation: a signaling target for
novel anti-cancer drug design

AUTHOR(S): Lerner, Edwina C.; Hamilton, Andrew D.; Sebti, Said M.

CORPORATE SOURCE: H. Lee Moffitt Cancer Center, Drug Discovery Program,
Department of Biochemistry and Molecular Biology,
University of South Florida, Tampa, FL, 33612, USA

SOURCE: Anti-Cancer Drug Design (1997), 12(4), 229-238

CODEN: ACDDEA; ISSN: 0266-9536

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal; **General Review**

LANGUAGE: English

AB A review with 55 refs. The cancer-causing activity of Ras requires the
prenylation of a cysteine fourth from its carboxyl terminus. Rational
design of peptidomimetics of the carboxyl terminal tetrapeptide
prenylation site on Ras resulted in pharmacol. agents capable of
inhibiting Ras process, selectively antagonizing oncogenic signaling and
suppressing human tumor growth in mouse models without side effects. This
mini-review describes the efforts of several groups to design, synthesize
and evaluate the biol. activities of farnesyltransferase and
geranylgeranyltransferase I inhibitors. Among the important issues that
will be discussed are the mechanism of action of these inhibitors and the
potential mechanisms of resistance to inhibition of K-Ras farnesylation.

CC 1-0 (Pharmacology)

IT **Antitumor agents**

Drug design

(drug design of Ras prenylation inhibiting anticancer agents)

IT 135371-29-8, Geranylgeranyltransferase I

RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(I; drug design of Ras prenylation inhibiting anticancer agents)

IT 135371-29-8, Geranylgeranyltransferase I

RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(I; drug design of Ras prenylation inhibiting anticancer agents)

L40 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:44904 HCAPLUS
DOCUMENT NUMBER: 126:139314
TITLE: Oncologic, endocrine & metabolic. Farnesyl-protein transferase inhibitors in early development
AUTHOR(S): Singh, Sheo B.; Lingham, Russel B.
CORPORATE SOURCE: Merck and Co., Inc., Rathway, NJ, 07065, USA
SOURCE: Expert Opinion on Investigational Drugs (1996), 5(12), 1589-1599
CODEN: EOIDER; ISSN: 0967-8298
PUBLISHER: Ashley Publications
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review, with 47 refs. Over the last decade the underlying mechanisms that cause tumorigenesis are progressively being elucidated. One potential mechanism includes the participation of farnesyl-protein transferase in promoting the effects of oncogenic forms of ras. Membrane localization of Ras is essential for ras-induced tumor formation. Farnesyl-protein transferase catalyzes the attachment of farnesyl to the carboxyl terminal cysteine residue of Ras. Genetic evidence indicates that unprenylated oncogenic Ras is soluble, cannot promote tumorigenesis and is apparently not deleterious to the cell. Several inhibitors of farnesyl-protein transferase are currently being tested in animal models of tumorigenesis. This review will focus on compds. that are presently being developed by Eisai, Banyu, Bristol-Myers Squibb, Merck, Roche/Genentech/University of Texas, Schering-Plough and the University of Pittsburgh.

CC 1-0 (Pharmacology)

IT **Antitumor agents**

Transformation, neoplastic

(development of farnesyl-protein transferase inhibitors for inhibition of tumorigenesis in relation to Ras)

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:570368 HCAPLUS
DOCUMENT NUMBER: 125:265162
TITLE: Farnesyltransferase inhibitors: a new class of cancer chemotherapeutics
AUTHOR(S): Koblan, K. S.; Kohl, N. E.; Omer, C. A.; Anthony, N. J.; conner, M. W.; deSolms, S. J.; Williams, T. M.; Graham, S. L.; Hartman, G. D.; et al.
CORPORATE SOURCE: Departments of Cancer Research, Medicinal Chemistry and Safety Assessment, Merck Research Laboratories, West Point, PA, 19486, USA
SOURCE: Biochemical Society Transactions (1996), 24(3), 688-692
CODEN: BCSTB5; ISSN: 0300-5127
PUBLISHER: Portland Press
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB Peptidomimetic farnesyltransferase inhibitors such as L-739,749 are a new class of cancer chemotherapeutic drugs that act by inhibiting function of oncogenic Ras protein. A review on the subject is also given; 26 refs.

CC 1-6 (Pharmacology)
IT **Neoplasm inhibitors**
(peptidomimetic cancer chemotherapeutic drugs as farnesyltransferase inhibitors)
IT 156511-34-1, L 739749 160141-09-3, L744832
RL: **BAC (Biological activity or effector, except adverse);** BSU
(Biological study, unclassified); **THU (Therapeutic use);** BIOL
(Biological study); **USES (Uses)**
(peptidomimetic cancer chemotherapeutic drugs as farnesyltransferase inhibitors)
IT 156511-34-1, L 739749 160141-09-3, L744832
RL: **BAC (Biological activity or effector, except adverse);** BSU
(Biological study, unclassified); **THU (Therapeutic use);** BIOL
(Biological study); **USES (Uses)**
(peptidomimetic cancer chemotherapeutic drugs as farnesyltransferase inhibitors)

L40 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:160722 HCAPLUS
DOCUMENT NUMBER: 124:249420
TITLE: Farnesyltransferase inhibitors and anti-Ras therapy
AUTHOR(S): Gibbs, Jackson B.; Kohl, Nancy E.; Koblan, Kenneth S.;
Omer, Charles A.; Sepp-Lorenzino, Laura; Rosen, Neal;
Anthony, Neville J.; Conner, Michael W.; DeSolms, S.
Jane; et al.
CORPORATE SOURCE: Department Cancer Research, Merck Research
Laboratories, West Point, PA, 19486, USA
SOURCE: Breast Cancer Research and Treatment (1996), 38(1),
75-83
CODEN: BCTRD6; ISSN: 0167-6806
PUBLISHER: Kluwer
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review, with 29 refs. The oncoprotein encoded by mutant ras genes is initially synthesized as a cytoplasmic precursor which requires post-translational processing to attain biol. activity; farnesylation of the cysteine residue present in the CaaX motif located at the carboxy-terminus of all Ras proteins is the critical modification. Once farnesylated and further modified, the mature Ras protein is inserted into the cell's plasma membrane where it participates in the signal transduction pathways that control cell growth and differentiation. The farnesylation reaction that modifies Ras and other cellular proteins having an appropriate CaaX motif is catalyzed by a housekeeping enzyme termed farnesyl-protein transferase (FPTase). Inhibitors of this enzyme have been prepared by several labs. in an effort to identify compds. that would block Ras-induced cell transformation and thereby function as Ras-specific anticancer agents. A variety of natural products and synthetic organic compds. were found to block farnesylation of Ras proteins in vitro. Some of these compds. exhibit antiproliferative activity in cell culture, block the morphol. alterations associated with Ras-transformation, and can block the growth of Ras-transformed cell lines in tumor colony-forming assays. By contrast, these compds. do not affect the growth or morphol. of cells transformed by the Raf or Mos oncoproteins, which do not require farnesylation to achieve biol. activity. The efficacy and lack of toxicity observed with FPTase inhibitors in an animal tumor model suggest that specific FPTase inhibitors may be useful for the treatment of some types of cancer.

CC 1-0 (Pharmacology)
IT **Neoplasm inhibitors**
(farnesyltransferase inhibitors and treatment of ras-dependent cancers)

L40 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:47215 HCAPLUS
DOCUMENT NUMBER: 124:105390
TITLE: Inhibitors of protein farnesylation: A new approach to
cancer chemotherapy
AUTHOR(S): Graham, Samuel L.
CORPORATE SOURCE: Department Medicinal Chemistry, Merck Research
Laboratories, West Point, PA, 19486, USA
SOURCE: Expert Opinion on Therapeutic Patents (1995), 5(12),
1269-85
CODEN: EOTPEG; ISSN: 1354-3776
PUBLISHER: Ashley Publications
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review, with 121 refs., of the types of compds. that are reported to
inhibit the enzyme protein farnesyltransferase and the biol. effects of
these compds. in vitro and in vivo. Topics discussed were: analogs of the
protein substrate (CaaX mimetics); analogs of farnesyl diphosphate (FPP
mimetics); bisubstrate analogs; and non-competitive inhibitors and
inhibitors of unreported mechanism. The antitumor activity of these
compds. centers around the interference with mutant oncogenic Ras
proteins.

CC 1-0 (Pharmacology)
IT **Neoplasm inhibitors**
(protein farnesylation inhibitors in cancer chemotherapy)
IT **Neoplasm inhibitors**
(protein farnesylation inhibitors in cancer chemotherapy)

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L5 1 SEA FILE=REGISTRY ABB=ON PLU=ON TAXANE/CN
L30 178659 SEA FILE=HCAPLUS ABB=ON PLU=ON ANTITUMOR AGENTS+OLD/CT
L64 125 SEA FILE=HCAPLUS ABB=ON PLU=ON L5(L) (BAC OR DMA OR PAC OR
PKT OR THU)/RL AND L30
L65 5 SEA FILE=HCAPLUS ABB=ON PLU=ON L64 AND REVIEW/DT NOT PY>1997

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L65 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:669181 HCAPLUS
DOCUMENT NUMBER: 127:287554
TITLE: Clinical overview of the taxanes
AUTHOR(S): Goldspiel, Barry R.
CORPORATE SOURCE: National Institutes of Health, Bethesda, MD,
20892-1196, USA
SOURCE: Pharmacotherapy (1997), 17(5, Pt. 2), 110S-125S
CODEN: PHPYDQ; ISSN: 0277-0008
PUBLISHER: Pharmacotherapy Publications
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 156 refs. Paclitaxel and docetaxel are taxane antineoplastic agents with broad antitumor activity. Since being introduced, they have become increasingly important in the treatment of a number of major solid tumors. Paclitaxel plus a Pt analog is now considered 1st-line therapy for advanced ovarian cancer, and both paclitaxel and docetaxel have significant activity as single agents in recurrent ovarian cancer. Docetaxel may be useful in some of these women with ovarian cancer who fail to progress after paclitaxel-containing treatments. Both drugs give significant response rates in the treatment of breast cancer and are options for patients with advanced disease, including anthracycline-refractory disease. Administration of taxanes in new combination regimens and as adjuvant therapy for breast cancer is under investigation; for example, the combination of paclitaxel and doxorubicin is highly active, and comparative studies of taxanes and anthracyclines should help clarify optimal treatment regimens in breast cancer. Both drugs have significant activity alone in the treatment of advanced non-small-cell lung cancer (NSCLC) and head and neck cancers. For the former, paclitaxel-cisplatin is now standard treatment in cooperative group combination therapy trials. As a result of its radiosensitizing properties, paclitaxel is undergoing extensive evaluation as combined modality treatment for advanced NSCLC and head and neck cancer. Both taxanes will probably be useful in combination regimens in head and neck cancer.

CC 1-0 (Pharmacology)

IT **Antitumor agents**

(clin. overview of the taxanes as)

IT 1605-68-1D, Taxane, derivs. 33069-62-4, Paclitaxel
114977-28-5, DocetaxelRL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(clin. antitumor effect of)

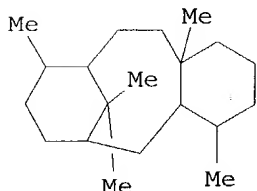
IT 1605-68-1D, Taxane, derivs.

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); **THU (Therapeutic use)**; BIOL
(Biological study); USES (Uses)
(clin. antitumor effect of)

RN 1605-68-1 HCAPLUS

CN 6,10-Methanobenzocyclodecene, tetradecahydro-4,9,12a,13,13-pentamethyl-,
(4R,4aR,6S,9R,10S,12aR)- (9CI) (CA INDEX NAME)



L65 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1995:764215 HCAPLUS

DOCUMENT NUMBER: 123:159932

TITLE: Preclinical antitumor activity of taxanes

AUTHOR(S): Rose, William C.

CORPORATE SOURCE: USA

SOURCE: Taxol: Science and Applications (1995), 209-35.
Editor(s): Suffness, Matthew. CRC: Boca Raton, Fla.
CODEN: 61PEAY

DOCUMENT TYPE: Conference; **General Review**

LANGUAGE: English

AB A review with 70 refs. In vitro and in vivo activities of taxol and taxotere and taxanes are discussed.

CC 1-0 (Pharmacology)

IT **Neoplasm inhibitors**

(preclin. antitumor activity of taxanes)

IT 1605-68-1D, Taxane, derivs. 33069-62-4, Taxol

RL: **BAC (Biological activity or effector, except adverse)**; BSU

(Biological study, unclassified); **THU (Therapeutic use)**; BIOL

(Biological study); USES (Uses)

(preclin. antitumor activity of taxanes)

IT 1605-68-1D, Taxane, derivs.

RL: **BAC (Biological activity or effector, except adverse)**; BSU

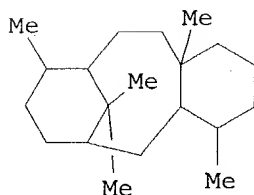
(Biological study, unclassified); **THU (Therapeutic use)**; BIOL

(Biological study); USES (Uses)

(preclin. antitumor activity of taxanes)

RN 1605-68-1 HCAPLUS

CN 6,10-Methanobenzocyclodecene, tetradecahydro-4,9,12a,13,13-pentamethyl-,
(4R,4aR,6S,9R,10S,12aR)- (9CI) (CA INDEX NAME)



L65 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:280269 HCAPLUS
DOCUMENT NUMBER: 122:106132
TITLE: Syntheses and structure-activity relationships of new
taxoids
AUTHOR(S): Ojima, Iwao; Park, Young Hoon; Fenoglio, Ivana;
Duclos, Olivier; Sun, Chung-Ming; Kuduk, Scott D.;
Zucco, Martine; Appendino, Giovanni; Pera, Paula; et
al.
CORPORATE SOURCE: Dep. Chem., State Univ. New York, Stony Brook, NY,
11794-3400, USA
SOURCE: ACS Symposium Series (1995), 583(Taxane Anticancer
Agents), 262-75
CODEN: ACSMC8; ISSN: 0097-6156
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB Review with 34 refs. A series of new taxoids are synthesized from
14 β -hydroxy-10-deacetylbaicatin III (14-OH-DAB). These new taxanes
possess strong cytotoxicities against human cancer cell lines, and at
least one of them possesses excellent antitumor activity in vivo.
Pseudo-taxoids bearing N-acylphenylisoserine side chain at C-14 are
synthesized, which are less active, but retain a certain level of
cytotoxicity. Novel nor-seco-paclitaxel and docetaxel analogs are
synthesized, which retain a certain level of activity despite the
destruction of the A ring. New analogs bearing cyclohexyl groups at the
C-3' and/or C-2 positions are synthesized and their cytotoxicity examined
The results clearly indicate that Ph group at C-3' or C-2 is not a
requisite for biol. activity. 3'-Isobutenyl and 3'-iso-Bu analogs of
docetaxel show excellent activity against a drug-resistant cancer cell
lines.

CC 30-0 (Terpenes and Terpenoids)
Section cross-reference(s): 1

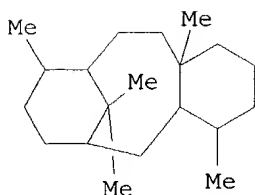
IT **Neoplasm inhibitors**
(syntheses and structure-activity relationships of new taxoids)

IT **1605-68-1DP, Taxane, derivs.**
RL: **BAC (Biological activity or effector, except adverse);** BSU
(Biological study, unclassified); SPN (Synthetic preparation); BIOL
(Biological study); PREP (Preparation)
(syntheses and structure-activity relationships of new taxoids)

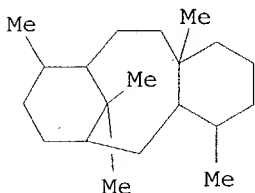
IT **1605-68-1DP, Taxane, derivs.**
RL: **BAC (Biological activity or effector, except adverse);** BSU
(Biological study, unclassified); SPN (Synthetic preparation); BIOL
(Biological study); PREP (Preparation)
(syntheses and structure-activity relationships of new taxoids)

RN 1605-68-1 HCAPLUS

CN 6,10-Methanobenzocyclodecene, tetradecahydro-4,9,12a,13,13-pentamethyl-,
(4R,4aR,6S,9R,10S,12aR)- (9CI) (CA INDEX NAME)



L65 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:569469 HCAPLUS
DOCUMENT NUMBER: 121:169469
TITLE: Paclitaxel and docetaxel: new anticancer agents
AUTHOR(S): Madelaine, I.; Faure, P.
CORPORATE SOURCE: Hop. Saint-Louis, Paris, 75010, Fr.
SOURCE: Journal de Pharmacie Clinique (1994), 13(1), 9-16
CODEN: JPCLDE; ISSN: 0291-1981
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: French
AB A review, with 57 refs. on taxanes as new anticancer agents.
CC 1-0 (Pharmacology)
IT **Neoplasm inhibitors**
(taxanes)
IT **1605-68-1D**, Taxane, derivs.
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); **THU (Therapeutic use)**; BIOL
(Biological study); **USES (Uses)**
(antitumor activity of)
IT **1605-68-1D**, Taxane, derivs.
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); **THU (Therapeutic use)**; BIOL
(Biological study); **USES (Uses)**
(antitumor activity of)
RN 1605-68-1 HCAPLUS
CN 6,10-Methanobenzocyclodecene, tetradecahydro-4,9,12a,13,13-pentamethyl-,
(4R,4aR,6S,9R,10S,12aR)- (9CI) (CA INDEX NAME)



L65 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:498892 HCAPLUS
DOCUMENT NUMBER: 121:98892
TITLE: Taxoids: a new class of cytotoxic agents
AUTHOR(S): Marty, M.; Extra, J M.; Giacchetti, S.; Cuvier, C.;
Espie, M.
CORPORATE SOURCE: Serv. d'Oncologie Med., Hop. St. Louis, Paris,
F-75010, Fr.

SOURCE: *Nouvelle Revue Francaise d'Hematologie* (1994),
36(SUPPL. 1), S25-S28
CODEN: NRFHA4; ISSN: 0029-4810

DOCUMENT TYPE: Journal; **General Review**

LANGUAGE: English

AB A review, with 17 refs., of the antitumor pharmacol. of the taxoids
paclitaxel and docetaxel.

CC 1-0 (Pharmacology)

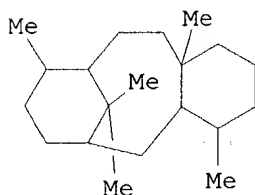
IT **Neoplasm inhibitors**
(taxoids paclitaxel and docetaxel as)

IT **1605-68-1D**, Taxane, derivs. 33069-62-4, Paclitaxel
114977-28-5, Docetaxel
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); **THU (Therapeutic use)**; BIOL
(Biological study); USES (Uses)
(neoplasm inhibition by)

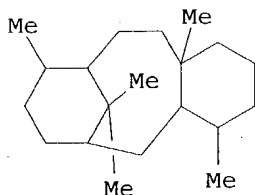
IT **1605-68-1D**, Taxane, derivs.
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); **THU (Therapeutic use)**; BIOL
(Biological study); USES (Uses)
(neoplasm inhibition by)

RN 1605-68-1 HCAPLUS

CN 6,10-Methanobenzocyclodecene, tetradecahydro-4,9,12a,13,13-pentamethyl-,
(4R,4aR,6S,9R,10S,12aR)- (9CI) (CA INDEX NAME)



L27 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 1605-68-1 REGISTRY
CN 6,10-Methanobenzocyclodecene, tetradecahydro-4,9,12a,13,13-pentamethyl-,
(4R,4aR,6S,9R,10S,12aR) - (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 6,10-Methanobenzocyclodecene, tetradecahydro-4,9,12a,13,13-pentamethyl-,
[4R-(4 α ,4a β ,6 α ,9 α ,10 α ,12a α)] -
CN **Taxane** (7CI, 8CI)
OTHER NAMES:
CN Taxan
MF C20 H36
LC STN Files: ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS, CA, CANCERLIT,
CAOLD, CAPLUS, CBNB, CEN, CIN, MEDLINE, PIRA, PROMT, TOXCENTER, USPAT2,
USPATFULL
DT.CA Caplus document type: Book; Conference; Dissertation; Journal; Patent
RL.P Roles from patents: BIOL (Biological study); MSC (Miscellaneous); OCCU
(Occurrence); PREP (Preparation); PROC (Process); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical
study); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation);
PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES
(Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological
study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP
(Preparation); PROC (Process); PRP (Properties); RACT (Reactant or
reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical
study); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation);
PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES
(Uses)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

273 REFERENCES IN FILE CA (1907 TO DATE)
147 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
273 REFERENCES IN FILE CAPLUS (1907 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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L8 1 SEA FILE=REGISTRY ABB=ON PLU=ON DESOXYEPOTHILONE A/CN
L30 178659 SEA FILE=HCAPLUS ABB=ON PLU=ON ANTITUMOR AGENTS+OLD/CT
L70 41 SEA FILE=HCAPLUS ABB=ON PLU=ON L8(L) (BAC OR DMA OR PAC OR
PKT OR THU)/RL AND L30
L71 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L70 AND REVIEW/DT NOT PY>1997

=> d l71 ibib abs hitind hitstr

L71 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:729 HCAPLUS

DOCUMENT NUMBER: 128:88685

TITLE: Metathesis vs metastasis: the chemistry and biology of the epothilones

AUTHOR(S): Finlay, Ray

CORPORATE SOURCE: Dep. Chemistry, The Skaggs Inst. for Chemical Biol.,
The Scripps Res. Inst., La Jolla, CA, 92037, USASOURCE: Chemistry & Industry (London) (1997), (24), 991-996
CODEN: CHINAG; ISSN: 0009-3068

PUBLISHER: Society of Chemical Industry

DOCUMENT TYPE: Journal; **General Review**

LANGUAGE: English

AB A review with 15 refs. on a recent entry onto the scene of potentially useful natural products, the epothilones A - E, providing valuable information for the fight against cancer via their interaction with microtubules.

CC 26-0 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1IT **Antitumor agents**

Stereoselective synthesis

(chemical and bioactivity of the epothilones)

IT **Antitumor agents**

(metastasis; chemical and bioactivity of the epothilones)

IT 152044-53-6P, Epothilone A 152044-54-7P, Epothilone B
186692-73-9P, Epothilone C 189453-10-9P, Epothilone D
201049-37-8PRL: **BAC (Biological activity or effector, except adverse)**; BOC
(Biological occurrence); BSU (Biological study, unclassified); SPN
(Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological
study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(chemical and bioactivity of the epothilones)

IT 186692-73-9P, Epothilone C

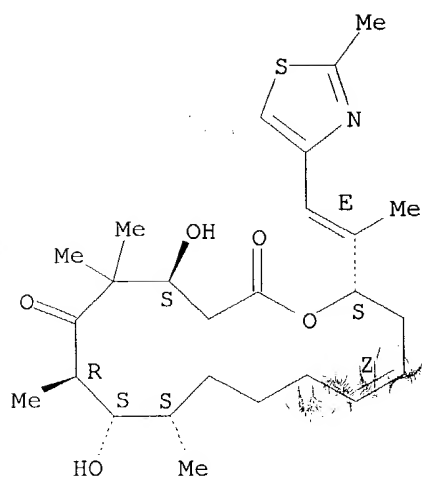
RL: **BAC (Biological activity or effector, except adverse)**; BOC
(Biological occurrence); BSU (Biological study, unclassified); SPN
(Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological
study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(chemical and bioactivity of the epothilones)

RN 186692-73-9 HCAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

Double bond geometry as shown.



REFERENCE COUNT:

26

THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN

RN 152044-54-7 REGISTRY

CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-
8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-
, (1S,3S,7S,10R,11S,12S,16R) - (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-
8,8,10,12,16-pentamethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-,
[1S-[1R*,3R*(E),7R*,10S*,11R*,12R*,16S*]] -

OTHER NAMES:

CN (-)-Epothilone B

CN EPO 906

CN **Epothilone B**

CN Patupilone

FS STEREOSEARCH

MF C27 H41 N O6 S

SR CA

LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BIOBUSINESS, BIOSIS,
BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CEN, CIN, EMBASE, IMSRESEARCH,
MRCK*, PHAR, PROMT, PROUSDDR, RTECS*, SYNTHLINE, TOXCENTER, USPAT2,
USPATFULL

(*File contains numerically searchable property data)

DT.CA Caplus document type: Conference; Dissertation; Journal; Patent

RL.P Roles from patents: BIOL (Biological study); CMBI (Combinatorial
study); FORM (Formation, nonpreparative); PREP (Preparation); PROC
(Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

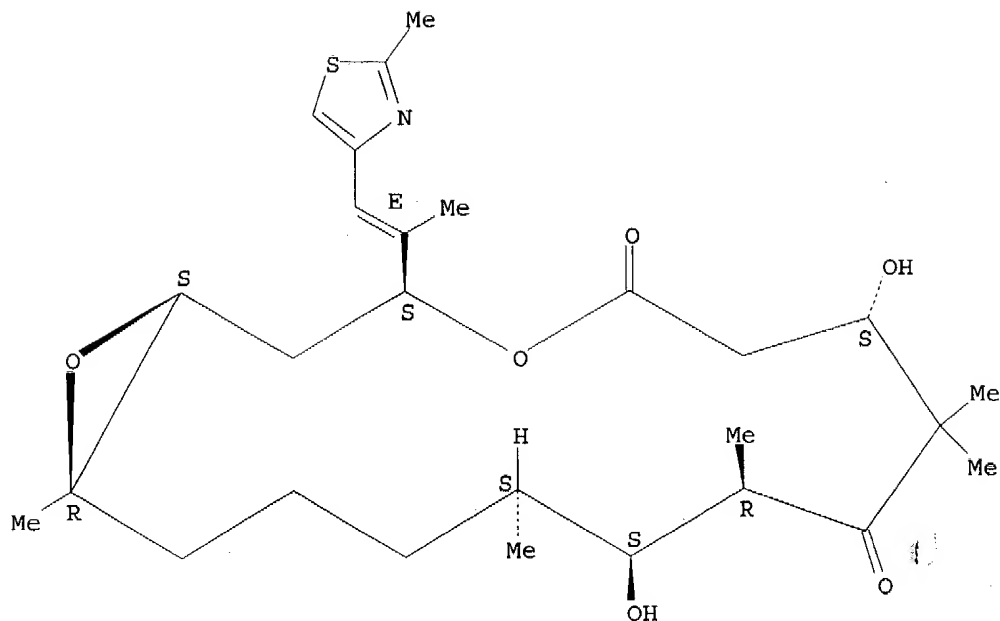
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological
study); PREP (Preparation); PROC (Process); USES (Uses)

RL.NP Roles from non-patents: BIOL (Biological study); FORM (Formation,
nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP
(Preparation); PROC (Process); PRP (Properties); RACT (Reactant or
reagent); USES (Uses)

RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological
study); MSC (Miscellaneous); PREP (Preparation); PRP (Properties); RACT
(Reactant or reagent); USES (Uses)

Absolute stereochemistry. Rotation (-).

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

302 REFERENCES IN FILE CA (1907 TO DATE)

30 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

302 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> d que 169

L7. 1 SEA FILE=REGISTRY ABB=ON PLU=ON EPOTHILONE B/CN
L30 178659 SEA FILE=HCAPLUS ABB=ON PLU=ON ANTITUMOR AGENTS+OLD/CT
L68 134 SEA FILE=HCAPLUS ABB=ON PLU=ON L7(L) (BAC OR DMA OR PAC OR
PKT OR THU)/RL AND L30
L69 2 SEA FILE=HCAPLUS ABB=ON PLU=ON L68 AND REVIEW/DT NOT PY>1997

=> d 169 ibib abs hitind hitstr 1-2

L69 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:729 HCAPLUS

DOCUMENT NUMBER: 128:88685

TITLE: Metathesis vs metastasis: the chemistry and biology of
the epothilones

AUTHOR(S): Finlay, Ray

CORPORATE SOURCE: Dep. Chemistry, The Skaggs Inst. for Chemical Biol.,
The Scripps Res. Inst., La Jolla, CA, 92037, USA

SOURCE: Chemistry & Industry (London) (1997), (24), 991-996
CODEN: CHINAG; ISSN: 0009-3068

PUBLISHER: Society of Chemical Industry

DOCUMENT TYPE: Journal; **General Review**

LANGUAGE: English

AB A review with 15 refs. on a recent entry onto the scene of potentially
useful natural products, the epothilones A - E, providing valuable
information for the fight against cancer via their interaction with
microtubules.

CC 26-0 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1

IT **Antitumor agents**
Stereoselective synthesis
(chemical and bioactivity of the epothilones)

IT **Antitumor agents**
(metastasis; chemical and bioactivity of the epothilones)

IT 152044-53-6P, Epothilone A **152044-54-7P**, Epothilone B
186692-73-9P, Epothilone C 189453-10-9P, Epothilone D 201049-37-8P
RL: **BAC (Biological activity or effector, except adverse)**; BOC
(Biological occurrence); BSU (Biological study, unclassified); SPN
(Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological
study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(chemical and bioactivity of the epothilones)

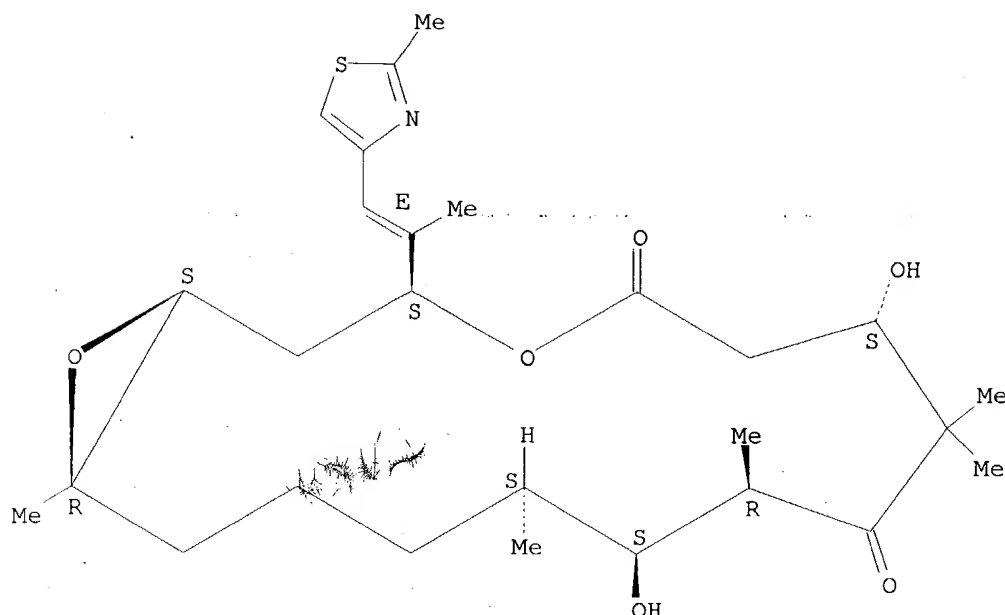
IT **152044-54-7P**, Epothilone B
RL: **BAC (Biological activity or effector, except adverse)**; BOC
(Biological occurrence); BSU (Biological study, unclassified); SPN
(Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological
study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(chemical and bioactivity of the epothilones)

RN 152044-54-7 HCAPLUS

CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-
8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-
, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

Double bond geometry as shown.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L69 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:455072 HCAPLUS
DOCUMENT NUMBER: 127:156078
TITLE: Epothilones: novel microtubule-stabilizing agents
AUTHOR(S): Bollag, Daniel M.
CORPORATE SOURCE: Merck Res. Lab., West Point, PA, 19486, USA
SOURCE: Expert Opinion on Investigational Drugs (1997), 6(7), 867-873
CODEN: EOIDER; ISSN: 0967-8298
PUBLISHER: Ashley Publications
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 44 refs. The past few years have witnessed the regulatory approvals of the anticancer microtubule stabilizing taxane drugs, Taxol and Taxotere which are rapidly gaining acceptance as important antineoplastic agents with potential against numerous solid tumor malignancies. Despite a basic understanding of the biochem. target of taxanes dating back nearly 20 yr, new classes of tubulin-binding microtubule polymerization enhancers were only reported in the last two years. Epothilones and discodermolide are newly discovered compds., which are structurally distinct from the taxanes, but which possess similar tubulin polymerizing and cell biol. effects. In the first studies reported, these compds. displayed similar or greater potencies than taxanes, and the epothilones may represent an advance over the taxanes in retaining toxicity against various taxane-resistant cell lines. This review summarizes the data published on epothilones and discodermolide and proposes further steps that could establish these new classes of compds. as potential second generation microtubule polymerization enhancers.

CC 1-0 (Pharmacology)
IT Antitumor agents

Microtubule

(epothilones and discodermolide as novel microtubule-stabilizing agents
in relation to anticancer activity in humans and laboratory animals)

IT 127943-53-7, Discodermolide 152044-53-6, Epothilone A

152044-54-7, Epothilone B

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(epothilones and discodermolide as novel microtubule-stabilizing agents
in relation to anticancer activity in humans and laboratory animals)

IT 152044-54-7, Epothilone B

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

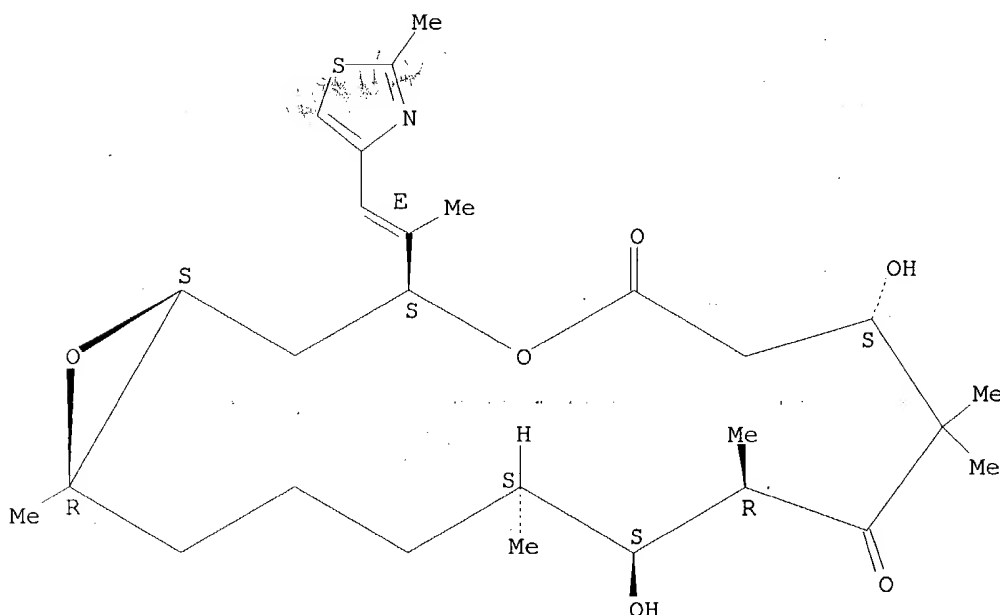
(epothilones and discodermolide as novel microtubule-stabilizing agents
in relation to anticancer activity in humans and laboratory animals)

RN 152044-54-7 HCAPLUS

CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-
8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-
, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

Double bond geometry as shown.



L28 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN

RN 152044-53-6 REGISTRY

CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, [1R*,3R*(E),7R*,10S*,11R*,12R*,16S*]-

OTHER NAMES:

CN (-)-Epothilone A

CN **Epothilone A**

FS STEREOSEARCH

DR 186692-57-9

MF C26 H39 N O6 S

SR CA

LC STN Files: ADISINSIGHT, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CEN, CIN, EMBASE, IMSDRUGNEWS, IMSRESEARCH, MRCK*, PHAR, PROMT, PROUSDDR, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)

DT.CA CAplus document type: Conference; Dissertation; Journal; Patent

RL.P Roles from patents: BIOL (Biological study); CMBI (Combinatorial study); FORM (Formation, nonpreparative); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)

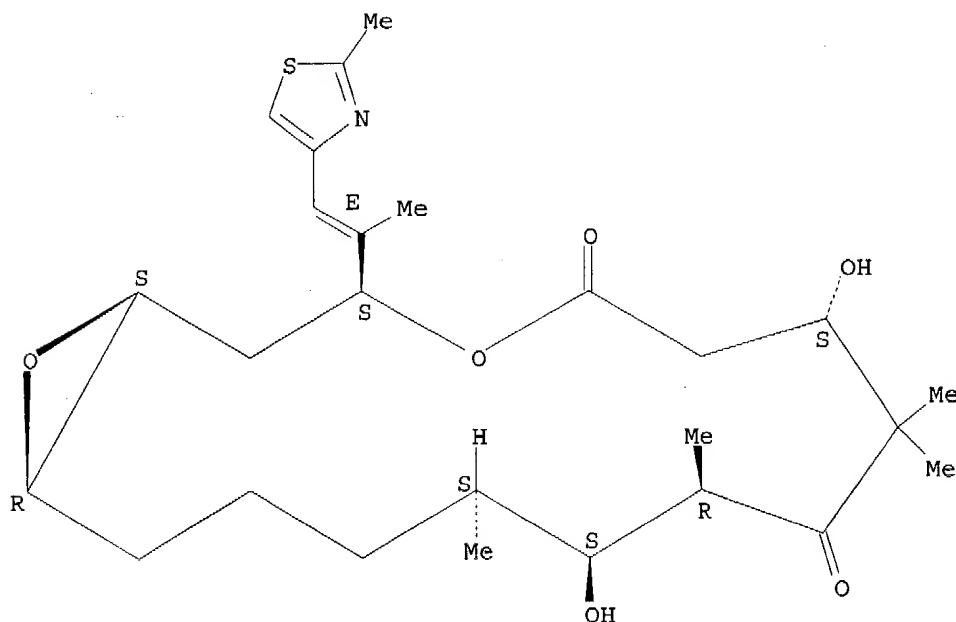
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

RL.NP Roles from non-patents: BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); MSC (Miscellaneous); PREP (Preparation); USES (Uses)

Absolute stereochemistry. Rotation (-).

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

272 REFERENCES IN FILE CA (1907 TO DATE)

30 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

273 REFERENCES IN FILE CAPLUS (1907 TO DATE)

Cook 09/445,054

July 26, 2004

109 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L34 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN

RN 186692-73-9 REGISTRY

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-
(9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[1-
methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, [4S-
[4R*,7S*,8R*,9R*,13Z,16R*(E)]]-

OTHER NAMES:

CN (-)-Deoxyepothilone A

CN (-)-Desoxyepothilone A

CN **Desoxyepothilone A**

CN Epo C

CN Epothilone C

FS STEREOSEARCH

MF C26 H39 N O5 S

SR CA

LC STN Files: BIOSIS, CA, CAPLUS, CASREACT, IMSRESEARCH, TOXCENTER, USPAT2,
USPATFULL

DT.CA Caplus document type: Dissertation; Journal; Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC
(Process); RACT (Reactant or reagent); USES (Uses)

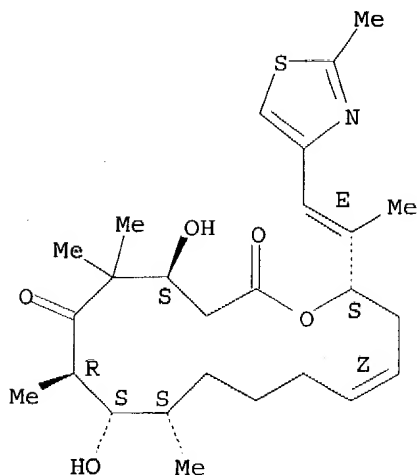
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological
study); PREP (Preparation); USES (Uses)

RL.NP Roles from non-patents: BIOL (Biological study); OCCU (Occurrence);
PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or
reagent); USES (Uses)

RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological
study); PREP (Preparation); USES (Uses)

Absolute stereochemistry. Rotation (-).

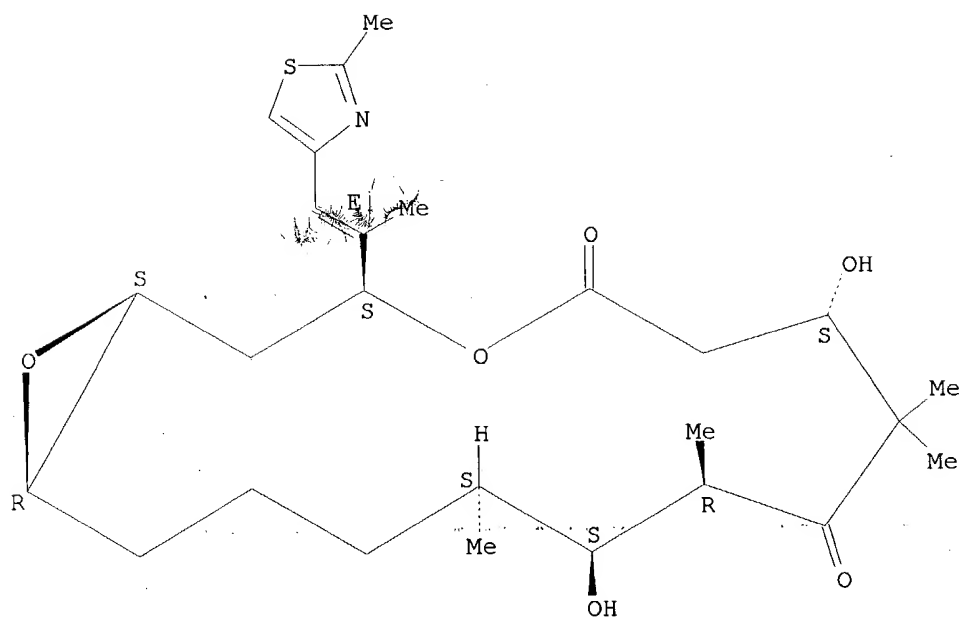
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

109 REFERENCES IN FILE CA (1907 TO DATE)

6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA



antineoplastic agents with potential against numerous solid tumor malignancies. Despite a basic understanding of the biochem. target of taxanes dating back nearly 20 yr, new classes of tubulin-binding microtubule polymerization enhancers were only reported in the last two years. Epothilones and discodermolide are newly discovered compds., which are structurally distinct from the taxanes, but which possess similar tubulin polymerizing and cell biol. effects. In the first studies reported, these compds. displayed similar or greater potencies than taxanes, and the epothilones may represent an advance over the taxanes in retaining toxicity against various taxane-resistant cell lines. This review summarizes the data published on epothilones and discodermolide and proposes further steps that could establish these new classes of compds. as potential second generation microtubule polymerization enhancers.

CC 1-0 (Pharmacology)

IT **Antitumor agents**

Microtubule

(epothilones and discodermolide as novel microtubule-stabilizing agents in relation to anticancer activity in humans and laboratory animals)

IT 127943-53-7, Discodermolide **152044-53-6**, Epothilone A

152044-54-7, Epothilone B

RL: **BAC (Biological activity or effector, except adverse)**; BSU

(Biological study, unclassified); **THU (Therapeutic use)**; BIOL

(Biological study); **USES (Uses)**

(epothilones and discodermolide as novel microtubule-stabilizing agents in relation to anticancer activity in humans and laboratory animals)

IT **152044-53-6**, Epothilone A

RL: **BAC (Biological activity or effector, except adverse)**; BSU

(Biological study, unclassified); **THU (Therapeutic use)**; BIOL

(Biological study); **USES (Uses)**

(epothilones and discodermolide as novel microtubule-stabilizing agents in relation to anticancer activity in humans and laboratory animals)

RN 152044-53-6 HCAPLUS

CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

Double bond geometry as shown.

(chemical and bioactivity of the epothilones)

IT 152044-53-6P, Epothilone A

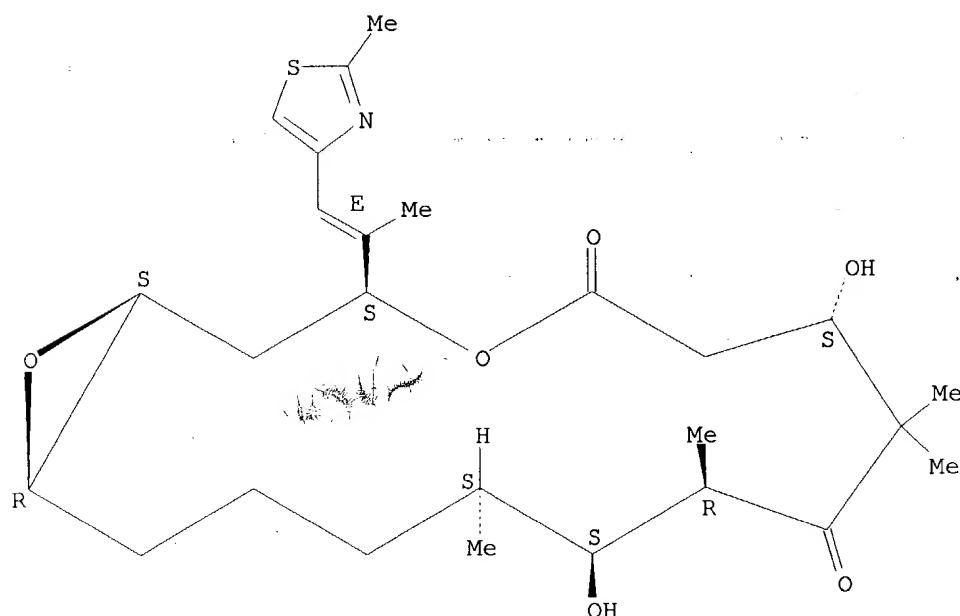
RL: **BAC (Biological activity or effector, except adverse)**; BOC
 (Biological occurrence); BSU (Biological study, unclassified); SPN
 (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological
 study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
 (chemical and bioactivity of the epothilones)

RN 152044-53-6 HCAPLUS

CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-
 tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-,
 (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

Double bond geometry as shown.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:455072 HCAPLUS

DOCUMENT NUMBER: 127:156078

TITLE: Epothilones: novel microtubule-stabilizing agents

AUTHOR(S): Bollag, Daniel M.

CORPORATE SOURCE: Merck Res. Lab., West Point, PA, 19486, USA

SOURCE: Expert Opinion on Investigational Drugs (1997), 6(7),
 867-873

CODEN: EOIDER; ISSN: 0967-8298

PUBLISHER: Ashley Publications

DOCUMENT TYPE: Journal; **General Review**

LANGUAGE: English

AB A review with 44 refs. The past few years have witnessed the regulatory
 approvals of the anticancer microtubule stabilizing taxane drugs, Taxol
 and Taxotere which are rapidly gaining acceptance as important

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L6 1 SEA FILE=REGISTRY ABB=ON PLU=ON EPOTHILONE A/CN
L30 178659 SEA FILE=HCAPLUS ABB=ON PLU=ON ANTITUMOR AGENTS+OLD/CT
L66 98 SEA FILE=HCAPLUS ABB=ON PLU=ON L6(L) (BAC OR DMA OR PAC OR
PKT OR THU)/RL AND L30
L67 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L66 AND REVIEW/DT NOT PY>1997

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L67 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:69781 HCAPLUS

DOCUMENT NUMBER: 128:188181

TITLE: The use of microtubule poisons on tumor cells

AUTHOR(S): Avila, J.

CORPORATE SOURCE: Cent. Biol. Mol. Univ. Autonoma de Madrid, Madrid,
28049, Spain

SOURCE: Cancer Journal (1997), 10(6), 315-318

CODEN: CANJEI; ISSN: 0765-7846

PUBLISHER: Association pour le Developpement de la Communication
Cancerologique

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A. review, with 20 refs. It appears that the use of microtubule poisons
is one of the most frequent therapeutic strategies for tumors. Drugs like
vinblastine and taxol have wide clin. use, although they have some
drawbacks. The discovery of new compds. such as epothilones could
overcome some of the problems found with the use of earlier drugs.

CC 1-0 (Pharmacology)

IT Antitumor agents
Microtubule

(use of microtubule poisons on tumor cells)

IT 64-86-8, Colchicine 865-21-4, Vinblastine 33069-62-4, Taxol
152044-53-6, Epothilone A

RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(use of microtubule poisons on tumor cells)

IT 152044-53-6, Epothilone A

RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

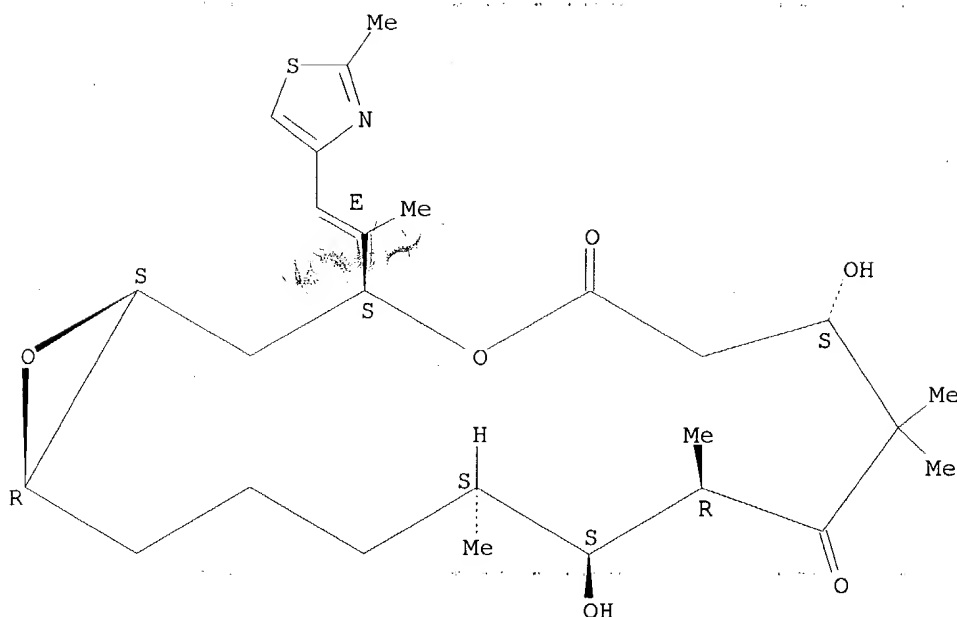
(use of microtubule poisons on tumor cells)

RN 152044-53-6 HCAPLUS

CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-
tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-,
(1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

Double bond geometry as shown.



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:729 HCAPLUS

DOCUMENT NUMBER: 128:88685

TITLE: Metathesis vs metastasis: the chemistry and biology of the epothilones

AUTHOR(S): Finlay, Ray

CORPORATE SOURCE: Dep. Chemistry, The Skaggs Inst. for Chemical Biol., The Scripps Res. Inst., La Jolla, CA, 92037, USA

SOURCE: Chemistry & Industry (London) (1997), (24), 991-996
CODEN: CHINAG; ISSN: 0009-3068

PUBLISHER: Society of Chemical Industry

DOCUMENT TYPE: Journal; **General Review**

LANGUAGE: English

AB A review with 15 refs. on a recent entry onto the scene of potentially useful natural products, the epothilones A - E, providing valuable information for the fight against cancer via their interaction with microtubules.

CC 26-0 (Biomolecules and Their Synthetic Analogs)

Section cross-reference(s): 1

IT **Antitumor agents**

Stereoselective synthesis

(chemical and bioactivity of the epothilones)

IT **Antitumor agents**

(metastasis; chemical and bioactivity of the epothilones)

IT **152044-53-6P**, Epothilone A 152044-54-7P, Epothilone B

186692-73-9P, Epothilone C 189453-10-9P, Epothilone D 201049-37-8P

RL: **BAC (Biological activity or effector, except adverse)**; BOC (Biological occurrence); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)